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(54) Title: METHOD FOR REMOVING RESIDUAL ADDITIVES FROM ELASTOMERIC ARTICLES (57) Abstract <p>A method for cleaning elastomeric articles comprising contacting the elastomeric article with at least one supercritical fluid under conditions and for a time sufficient to remove the phthalates and/or polynuclear aromatic hydrocarbons (PAHs) contained therein. Elastomeric articles having a reduced phthalate and/or PAH content prepared by the above method are also claimed. Such elastomeric articles having reduced phthalate contents can be utilized as gaskets, valves, seats, flaps or plugs in metered dose delivery devices such as aerosols for demanding medicinal and pharmaceutical uses.</p>		

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METHOD FOR REMOVING RESIDUAL ADDITIVES FROM ELASTOMERIC ARTICLES.

10 **BACKGROUND**

Certain elastomeric articles, ie. gaskets, valves and seats used in aerosol containers, are designed as part of the container for the efficacious delivery of pharmaceutically active compounds, ie. medicaments. As a matter of cost and convenience, such articles are derived using elastomeric materials such as elastomeric rubber and the like, specifically formulated with ingredients that enable the article to meet numerous demanding toxicological, chemical, and physical requirements. For example, gaskets and valves made of rubber are typically formulated with about six to twelve ingredients, including

15 monomers, polymers, organic solvents, organic plasticizers, antioxidants, antiozonants, curing agents, accelerators, pigments, tackifiers, reinforcing materials and inorganic fillers such as carbon black. Nearly all cured or finished articles will inherently contain small amounts of residual components derived from these ingredients. These

20 inherent residual components or impurities are not necessary for performance of the article but can potentially interact with the medicament or other excipients in the formulation, leading to reduced pharmaceutical dosing. Such impurities could also interact with the container, causing it to malfunction, such as by blocking a nozzle orifice.

30 A paper by A. Figazette et al., Analysis for Extractables From Nitrile Rubber Components in Metered Dose Inhalers, Pharmaceutical Analysis Department, SmithKline Beecham Pharmaceuticals, King of Prussia, Pennsylvania, was presented at the Symposium, "Regulatory Issues in Aerosol Drug Development", June 12-14, 1991 in Arlington

35 Virginia by the University of Kentucky College of Pharmacy. Figazette et

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al stated that contamination of pharmaceutical aerosols by substances leached from elastomeric valve assemblies in metered dose inhalers is a potentially serious problem. The authors present evidence that numerous extractables could be detected in valves from various suppliers, demonstrating a need for cleaner valve rubbers with fewer leachable extractants. One class of impurities is known as the polynuclear aromatic hydrocarbons (PNAs or PAHs). Another class of impurities is known as non-PAHs, including phthalates derived from plasticizers employed during processing. Presently, conventional methods for removing PAHs and non-PAHs from rubber articles involves liquid-solid extraction and refluxing using either conventional solvents or fluorocarbon type solvents (eg. freons). However, these conventional method are deemed unsatisfactory for preparing purified elastomeric articles using the newer, environmentally safer fluorohydrocarbons propellants such as HFC-134A, HFC-226a and HFC-227, for the following reasons. First, these conventional methods have the disadvantage of incurring high expenses for special handling and safety precautions, and for special buildings, rooms and equipment due to the explosive nature of the newer propellants, necessitating the need to use explosion-proof equipment. Second, these conventional methods have the further disadvantage of superficially cleaning primarily the outer surface of the article, leaving impurities in the interior of the article.

Clearly, it would be desirable to provide an improved method for cleaning elastomeric articles by removal of the impurities contained therein, particularly for highly demanding pharmaceutical and medicinal uses. It would also be desirable to provide a method for preparing such articles which would meet governmental regulatory requirements (ie. Food and Drug Administration). Furthermore, it would also be desirable to provide a method for cleaning elastomeric articles that is occupationally and environmentally safer, simpler, more rapid and less expensive than known conventional methods.

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SUMMARY OF THE INVENTION

The present invention is directed towards a method for cleaning elastomeric articles comprising contacting the elastomeric article with at least one supercritical fluid under conditions and for a time sufficient to
5 remove the phthalates and/or polynuclear aromatic hydrocarbons (PAHs) contained therein. Selected phthalates include dibutyl phthalate or diisooctyl phthalate. Preferably the supercritical fluid is carbon dioxide.

The present invention is also directed toward an elastomeric article having a reduced phthalate and/or PAH content prepared by the
10 above method. Preferably the elastomeric article is made of rubber, preferably nitrile rubber. Also preferred is that the elastomeric article is a rubber gasket, valve, seat, flap or plug, such as those employed in metered dose delivery devices, which use chlorofluorohydrocarbons or fluorohydrocarbons as propellants. The propellant can be a
15 chlorofluorohydrocarbon such as PDP-11 or a fluorohydrocarbon such as HFC-134A, HFC-226A or HFC-227.

One advantage of the present invention is that it provides an elastomeric article for medicinal or pharmaceutical use whose phthalate and/or PAH content is significantly lower than similar articles cleaned by
20 conventional procedures.

A second advantage of the present invention is that it provides a simpler and faster method for removing phthalate and/or PAH impurities from an elastomeric article, compared to conventional procedures.

A third advantage of the present invention is that it provides a
25 method for removing phthalate and/or PAH impurities from elastomeric articles that is less expensive than by other known procedures.

A fourth advantage of the present invention is that it provides an occupationally and environmentally safer method for removing phthalate and/or PAH impurities from elastomeric articles, compared to
30 conventional procedures.

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DETAILED DESCRIPTION OF THE INVENTION

Throughout the specification, the terms "purifying" and "cleaning" are used interchangeably.

As defined by Gessner G. Hawley, The Condensed Chemical Dictionary, 10th Edition, Van Nostrand Reinhold Co., New York, (1981), 1135 pp., the term "elastomer" as originally defined by Fisher (1940), refers to synthetic thermosetting high polymers having properties similar to those of vulcanized natural rubber, namely, the ability to be stretched to at least twice their original length and to retract very rapidly to approximately their original length when released. Among the better known elastomers are styrene-butadiene copolymer, polychloroprene (neoprene), nitrile rubber, butyl rubbers such as the non-halogenated rubbers, the chlorinated rubbers and brominated rubbers; polysulfide rubber ("Thiokol"), cis-1,4-polyisoprene, ethylene-propylene terpolymers (EPDM rubber), silicone rubber and polyurethane rubber. These can be cross-linked with sulfur, peroxides or similar agents. The term also includes uncross-linked polyolefins that are thermoplastic, generally known as TPO rubbers. Their extension and retraction properties are notably different from those of thermosetting elastomers, but they are well adapted to specific uses such as specialized mechanical products.

Also as defined by The Condensed Chemical Dictionary, above, the term "rubber" refers to any of a number of natural or synthetic high polymers having unique properties of deformation (elongation or yield under stress) and elastic recovery after vulcanization with sulfur or other cross-linking agent, which in effect changes the polymer from thermoplastic to thermosetting. The yield or stretch of the vulcanized material ranges from a few hundred to over 1000 per cent. The deformation after break, called "permanent set" is usually taken as the index of recovery. It ranges from 5 to 10% for natural rubber to 50% or more for some synthetic elastomers, and varies considerably with the state of vulcanization and the pigment loading. Representative rubbers include nitrile rubbers or neoprene, GR-S rubbers, polyisoprene, polybutadienes, and polysiloxanes.

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The term "propellants" refers to both compressible and incompressible gases used to expel the contents of containers in the form of aerosols, and include freons, fluorohydrocarbons, hydrocarbon gases such as butane and propane, carbon dioxide (CO₂), nitrogen (N₂), oxygen (O₂) and nitrous oxide (N₂O).

Such elastomeric materials can be useful for preparing articles for medical or pharmaceutical use such as rubber gaskets, valves, seats, flaps, stoppers and plugs used in aerosol containers, atomizers, pump sprays, droppers and other metered dose devices. Another use for such materials would be for stoppers used to cap vials, bottles, infusion bags, syringes, blood collection tubes and parenteral containers. And yet another use for such materials would be for septa used in analytical equipment such as injection ports of gas chromatographs. Other elastomeric materials include those used for implantation devices such as heart valves, limb joints, breast implants, intravenous and intestinal tubing, dental retainers and pharmaceutical containers. Another application could be for devices which are contacted with the mouth such as baby nipple, toothpicks, mouthguards used in sports, scuba diving mouthpieces, feed tubes, tracheal tubes and thermometers.

An apparatus for supercritical extraction is made up of an extraction cell, preferably cylindrical, which is housed in a chamber for controlling temperatures and pressures. At least one supercritical fluid (ie. extracting mobile phase), such as CO₂, is pumped into the extraction cell, through a pressure regulating restrictor to maintain back pressure and into a vessel which serves as a trap. As the supercritical fluid passes through the elastomeric article containing phthalate and/or PAH impurities, the supercritical fluid removes the phthalate and/or PAH impurities from the elastomeric article, leaving behind an elastomeric article whose phthalate and/or PAH content is significantly reduced. As the supercritical fluids containing the phthalate and/or PAH impurities leave the chamber, the fluids transform into a gas, which can be passed through or injected (ie. bubbled) into a trapping vessel.

The use of supercritical fluid extraction for analytical purposes is known. For example, in Supercritical Fluid Extraction and

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Chromatography, edited by Bonnie A. Charpentier and Michael R. Sevenants, ACS Symposium Series 366, by B. Wright et al., in Chapter 3: "Analytical Supercritical Fluid Extraction Methodologies" (1988), the authors teach that several polycyclic aromatic hydrocarbons (PAHs) were extracted from a chromatographic resin, ie. XAD-2, superficially spiked with several PAHs, using carbon dioxide at 325 bar and 50°C for 7 minutes. However, this reference fails to describe a process for removing phthalate and/or PAH impurities from an elastomeric article whose phthalates and/or PAHs have been integrated throughout the entire matrix of the elastomer article as a result of mixing, heating and curing steps involved in preparation of the elastomeric article.

The elastomeric article can be contacted with at least one supercritical fluid under conditions effective to extract phthalate and/or PAH impurities from the elastomeric article. The contacting of the article with the supercritical fluid can be carried out at temperatures ranging from about ambient to below the temperature resulting in degradation of the elastomer, such as from about 25°C to about 300°C, preferably from about 25°C to about 50°C, more preferably from about 30° to 35°C. The pressure at which the article can be contacted with the supercritical fluid can range from about 50 atmospheres (atm) to about 400 atm, preferably from about 100 to about 400 atm. The elastomeric article should be contacted with at least one supercritical fluid for a time sufficient to reduce the phthalate and/or PAH impurities to the desired level. Preferably the contacting is carried out for greater than one hour, more preferably for greater than two hours, most preferably about 4 hours or more. Generally, the longer contacting times with the supercritical fluid(s) allows for higher extraction of phthalates and/or PAHs.

The supercritical fluid employed in the present process can be one or more of any of those described in U.S. Patent 4,749,522. Representative extracting (solvating) mobile phase components include the elemental gases such as helium, argon, nitrogen and the like; inorganic compounds such as ammonia, carbon dioxide, nitrous oxide, water, and the like; and organic compounds. Suitable organic

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compounds include C-1 to C-5 alkanes such as propane and butane; alkyl halides such as monofluoromethane, carbon tetrachloride, chloroform, methylene chloride; aromatics such as xylene, toluene and benzene; aliphatics such as C-5 to C-20 alkanes including hexane, heptane and octane; C-1 to C-10 alcohols such as methanol, ethanol, propanol, butanol and isopropanol; ethers or acetone. Where more than one supercritical fluid is employed, the supercritical fluid employed in the larger amount, ie. greater than 50% on a volume basis, is considered to be the main solvent. If three or more supercritical fluids are employed, the main solvent will be that making up the largest proportion in the mixture. Co-solvent supercritical fluids which can supplement and tend to modify the solvating properties of the main supercritical fluid are employed in lower amounts relative to the main supercritical fluid, generally from about one to less than 50% on a volume basis, preferably from about one to about 10% relative to the main supercritical fluid. The co-solvent supercritical fluid employed in the present process should be compatible with the main supercritical fluid and also be capable of at least partially dissolving some of the impurities being extracted. Suitable co-solvents for use in conjunction with the supercritical fluid include any of those cited above for the main supercritical fluid or mixtures thereof.

One representative method for determining the phthalate and/or PAH content of an article cleaned by the present process is as follows. The elastomeric article to be tested is immersed or refluxed for a certain period of time with a solvent or solution matched for the environment in which the elastomeric article will be used. For example, elastomeric gaskets and seals used in aerosols can be immersed for about one to three weeks in an aerosol propellant, such as Freon11, Freon12, HFC-134A, HFC-226A or HFC-227. After the immersion period, the amount of phthalates and/or PAHs in the resultant solution (ie. propellant or residue thereof) is determined. Generally, the fewer phthalates and/or PAHs found in the resultant solution, the purer or "cleaner" is the elastomeric article. Similarly, the greater the amount of phthalates

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and/or PAHs found in the resulting solution corresponds to a higher content of phthalate and/or PAH impurities in the elastomeric article.

Phthalate impurities which can be extracted from an elastomeric article include those of the formula $C_6H_4(COOR)_2$ wherein R represents C-1 to C-12 alkyl such as for example methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl, octyl, isooctyl, decyl and the like. Other non-PAH impurities which can also be removed with the present process include 2-mercaptobenzothiazole (2-MCBT), N-cyclohexyl-2-benzthiazyl sulphenamide (CBS), nitrosamines, residual oligomers and certain plasticizers such as waxes, esters, stearates and phthalates such as dioctyl phthalate.

PAH impurities which can be extracted from an elastomeric article with the present process include those designated in U.S. Environmental Protection Agency Method 8310 - Polynuclear Aromatic Hydrocarbons, pp 8310-1 to 8310-13:

acenaphthene, acenaphthylene, anthracene, benzo(a)anthracene, benzo(a)pyrene, benzo(b)pyrene, benzo(e)pyrene, benzo(b)fluoranthene, benzo(ghi)perylene, chrysene, benzo(k)fluoranthene, dibenz(a,h)acridine, dibenz(a,j)acridine, dibenzo(a,h)anthracene, dibenzo(c,g)carbazole, dibenzo(a,e)pyrene, dibenzo(a,h)pyrene, dibenzo(a,i)pyrene, fluoranthene, fluorene, indeno(1, 2, 3-cd)pyrene, 3-methylcholanthrene, naphthalene, perylene, phenanthrene, pyrene or triphenylene.

After the immersion period is completed, impurities in the resultant solution can be analyzed using conventional analytical procedures, such as liquid chromatography, capillary chromatography, gas chromatography, and the like. Representative procedures to analyze for impurities in the resultant solution are provided below. Other analytical procedures such as supercritical fluid extraction (SFE) can be employed to analyze the solvent or propellant, especially where a particular impurity cannot be satisfactorily detected by conventional procedures.

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Analytical Procedure No. 1. Analysis for Phtalates

A pressurized aerosol can is cooled in a freezer for one hour. The freon propellant contained therein is slowly vented from each can via a slow incision made at the top of the can. Following the complete
5 removal of the freon propellant, the valve assembly is removed and discarded. Each can is then rinsed with one milliliter (mL) of dichloromethane containing 7.3 mg/mL of N-tetradecane, which serves as a volume indicator (ie. internal standard). The resultant
10 dichlormethane extract is then injected into and analyzed using a gas-chromatographic/ mass spectroscopic system.

Analytical Procedure No. 2. Liquid chromatography with Fluorescence Detection for Analyzing PAH

This Food and Drug Administration (FDA) validated procedure uses a flow injection analysis (FIA) system made of a high performance
15 liquid chromatography pump, an auto-injector, a fluorescence detector (filter or monochromator) set at the absorption maximum of anthracene at 250 nanometers (nm) and emission maximum at 397 nm, or use Kodak Wrattan filters No. 30, 34 or 39 or equivalent as emission filters, and chart recorder. The mobile phase is acetonitrile set at a flow rate of
20 one milliliter per minute. A series of standards ranging from a concentration of 5 parts per billion (ppb) to 500 ppb is prepared using anthracene in acetonitrile. From the standards, a response curve is determined by plotting the response generated by the fluorescence detector versus varying concentrations of the anthracene standards.
25 The sample, pressurized aerosol can is cooled in a dry ice/methanol bath and the top of the can is removed. The contents of the can and rinses of the valve assembly and empty can are filtered into a volumetric flask. After the propellant has evaporated, the volumetric flask is diluted to volume with acetonitrile or methylene chloride. The resulting solution
30 is analyzed on the FIA for anthracene and the results are quantitatively measured by comparison with the standard response curve.

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Analytical Procedure No. 3. Gas chromatography for Analyzing PAHs

This Environmental Protection Agency (EPA) procedure uses a system made of a PTE-5 QTM fused silica capillary column having dimensions of 15 meters (m) by 0.53 millimeters (mm) internal diameter (I.D.) and a flame ionization detector (FID). Helium is used as the carrier gas at a flow rate of 10 mL per minute. A series of 19 standards are prepared, each standard containing a specific PAH in methylene chloride in a concentration of 1.2 nanograms (ng) per microliter (μ L). The column temperature is increased to 85°C and held at this temperature for four minutes; then increased at a rate of 15°C per minute to 300°C and held for two minutes. The sample, pressurized aerosol can is cooled in a dry ice/methanol bath and the top of the can is removed. The contents of the can and rinses of the valve assembly and empty can are filtered into a volumetric flask. After the propellant has evaporated, the volumetric flask is diluted to volume with acetonitrile or methylene chloride. The resultant solution is analyzed on the gas chromatograph for the presence of any of the 19 PAHs.

It is highly desirable that the integrity of the article being cleaned of phthalates and/or PAHs is maintained. Thus, the present invention is not directed toward cleaning articles whose utility would be destroyed by exposure to supercritical fluids. For example, exposing a patch containing an adhesive to supercritical fluids would render the patch ineffective by dissolving or removing the adhesive.

In addition to removing phthalate and/or impurities, the present method has the advantage of providing an elastomeric article having a significantly reduced phthalate and/or PAH content whose physical properties are still maintained. Maintaining and verifying the retention of certain physical properties following cleaning is useful to assure proper mechanical functioning of the article. For example, a gasket or valve component can be evaluated for durometer (ie. hardness), tensile strength and elongation or compression set. Hardness can be evaluated with any suitable hardness tester with the desired sensitivity, using procedures such as described in ASTM-D-1415-68, Part - 68, July 1973 - International Hardness of Vulcanized Rubber or ASTM D-2240-

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75. Tensile strength and elongation can be evaluated with any suitable tensometer and extensometer, using procedures such as ASTM D-412-75. Compression set can be evaluated with any suitable compression set device, using procedures as described in ASTM D395-78.

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**EXAMPLE - Cleaning of Rubber Valve Components for Aerosols:
Removal of Phthalates and PAHs**

a) Supercritical Fluid Cleaning Using CO₂

10 To a ten mL stainless steel extraction cell is added one gram of nitrile rubber valve components. The operating conditions for supercritical cleaning are as follows:

Head Space Filler:	Helium
Restrictor Flow :	500 mL/min
Extracting Mobile Phase (ie. supercritical fluid):	Supercritical fluid grade CO ₂
Oven Temperature:	35°C
Pressure Program:	a. 100 atm. for 2 minutes b. 200 atm. for 2 minutes c. 225 atm. for 2 minutes d. 250 atm. for 2 minutes e. 275 atm. for 2 minutes f. 300 atm. for 240 minutes
Total Extraction Time:	1, 2 or 4 hours

15 **b) Measuring Phthalates and Other Impurities**

Various groups of nitrile rubber valve components are tested for phthalate impurities. One group of valve components represents the control, which receives no cleaning after manufacture of the valve component. A second group of valve components is cleaned conventionally by refluxing the valve components in Freon P11 for 72 hours, followed by
20 air drying. A third group of valve components is cleaned using the method of a) Supercritical Fluid Cleaning Using CO₂, above. Each

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group of nitrile rubber valve components is placed into a 10 mL aerosol container and immersed in 15 g of Freon 11. The containers are sealed and maintained at 40°C for two weeks. The containers are opened and the Freon is evaporated. The chemical residue in the container is

5 analyzed for phthalate impurities by a suitable analytical procedure.

Table I. Assay of Impurities Found in Extracts From Unprocessed Rubber, Conventionally Cleaned Rubber and Supercritical Fluid (SFE) Cleaned Rubber Used for Aerosol Seals and Gaskets

Extracted Impurity	Un-processed Rubber	Conventionally Cleaned Rubber	SFE-Cleaned Rubber		
			μg in extract-----		
			1 hrs	2 hrs	4 hrs
Cyclohexyl Isothiocyanate	7	<0.1	26	1	0.1
2,6-Di-t-butyl-4-methylpheno	<0.1	<0.2	<0.1	0.2	<0.1
2-Cyanoethyldimethyl-dithiocarbamate	67	0.1	71	4	0.2
Dibutyl phthalate	8	0.7	6	<0.1	0.1
2,2-Methylene-bis-(4-methyl-tert-butyl phenol)	6	7	3	12	6
Octadecanoic Acid	22	11	27	12	3
Carbamodithioic Acid Ester ^a	2	<0.1	<0.1	<0.1	<0.1
Unknown A	7	<0.1	0.4	<0.1	<0.1
Unknown B	2	<0.1	1	<0.1	<0.1
Unknown C	16	2	9	2	0.3
Unknown D	7	11	2	47	0.8
Diisooctyl Phthalate	28	9	6	3	0.1
High boiling aliphatics	11	2	4	6	2
Total mg Detected	183	43	155.4	87.2	19.8

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The results in Table 1 demonstrate that of the three rubbers tested, the 4-hour SFE-cleaned rubber had the lowest amounts of extractable impurities (ie. 19.8 mg) compared with the unprocessed (183 mg) and conventionally cleaned rubbers (43 mg). Also, the 4-hour SFE-cleaned rubbers had the lowest amounts of phthalates. For example, rubbers had dibutylphthalate and diisooctyl phthalate amounts which were 7- and 90-fold lower, respectively, than the rubbers conventionally cleaned using solvent extraction with Freon 11.

10

Table II. Physical Properties of Supercritical Fluid (SFE) Cleaned Rubber Prepared from Unprocessed Rubber Used for Aerosol Seals and Gaskets

	Change in Weight	Change in Hardness	Change in Physical Properties
Unprocessed Rubber	No change	No change	No change
4 hr SFE-Cleaned Rubber	- 4.00 mg	No change	No change
2 hr SFE-Cleaned Rubber	-3.13 mg	No change	No change
1 hr SFE-Cleaned Rubber	-2.29 mg	No change	No change

15 The results in Table II demonstrate that the SFE-cleaned rubbers incurred a loss in weight, reflecting a significant loss of impurities from the rubber matrix. However, despite this significant weight loss, no change for either hardness or the physical properties of the SFE-cleaned rubbers was observed.

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Table III. Assay of Impurities: Non-Volatile Residues and Total Polynuclear Aromatic Hydrocarbon Content (Per Anthracene Equivalents) Found in Extracts From Unprocessed Rubber,
 5 Conventionally Cleaned Rubber Used for Aerosol Seals and Gaskets

	Non-Volatile Residues (Peak Area Counts/mg rubber)	PAH Content (ppb of PAHs/mg Rubber)
Unprocessed Rubber	2024	10
Conventional Cleaning	747	7
4 hr SFE-Cleaned Rubber	458	3
2 hr SFE-Cleaned Rubber	1443	15
1 hr SFE-Cleaned Rubber	13,774	13

The results in Table III demonstrate that the 4 hour SFE-cleaned rubbers had the lowest total polynuclear aromatic hydrocarbon content (ie. 3
 10 ppb/mg rubber) as compared to either the unprocessed rubber (ie. 7 ppb/mg rubber) or the conventionally cleaned rubbers (10 ppb/mg rubber). Similarly, the 4 hour SFE-cleaned rubbers had the lowest non-volatile residues (ie. 458 area counts/mg rubber) of all the rubbers tested.

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WE CLAIM:

1. A method for cleaning elastomeric articles comprising contacting the elastomeric article with at least one supercritical fluid under conditions and for a time sufficient to remove the phthalates and/or polynuclear aromatic hydrocarbons (PAHs) contained therein.
2. The method of claim 1 wherein the phthalate being removed is dibutyl phthalate or diisooctyl phthalate.
3. The method of claims 1-2 wherein the supercritical fluid is carbon dioxide.
4. The method of claims 1-3 wherein the article is contacted with a supercritical fluid for about 4 hours or more.
5. An elastomeric article having a reduced phthalate and/or PAH content prepared by any of the methods of claims 1-4.
6. The elastomeric article of claim 5 made of rubber.
7. The elastomeric article of claims 5-6 made of nitrile rubber.
8. The elastomeric article of claims 5-7 which is a rubber valve, seat, flap, stopper or plug.
9. The elastomeric article of claims 5-8 which is a rubber gasket, valve, seat, flap, stopper or plug in combination with a metered dose delivery device.
10. The elastomeric article of claims 5-9 which is a rubber gasket, valve, seat, flap, stopper or plug in combination with an aerosol container containing chlorofluorohydrocarbons or fluorohydrocarbon propellants.

INTERNATIONAL SEARCH REPORT

PCT/US 92/10742

International Application No

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int.Cl. 5 C08J7/02; B01D11/02; //C08J7/02,C08L21/00		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl. 5	C08J ; B01D ; C08F	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	FR,A,2 638 098 (TOYO ENGINEERING CORPORATION) 27 April 1990 see page 11; example 1 see claims 1,3,5,7	1-10
A	DE,A,3 938 877 (BASF) 29 May 1991 see column 4; example 1 see claim 1	1-10
<p>¹⁰ Special categories of cited documents : ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search		Date of Mailing of this International Search Report
02 APRIL 1993		14. 05. 92
International Searching Authority		Signature of Authorized Officer
EUROPEAN PATENT OFFICE		OU DOT R.

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

US 9210742
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The members are as contained in the European Patent Office EDP file on
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